REMARKS

Applicants note with appreciation that claim 44 has been allowed. Upon entry of the present amendments, claims 44-49 will be pending in the application. Claims 1, 2, 4, 29 and 32 have been canceled. Claims 46-49 have been added. Support for these new claims can be found throughout the specification as filed, *e.g.*, at least in claims 29 and 32 as originally filed. Claim 45 has been amended. Support for the amendments to claim 45 can be found throughout the specification as filed, *e.g.* in at least page 50, lines 21-22; and page 53, line 24 through page 54, line 12. No new matter is added.

Election/Restrictions

Applicants thank the Examiner for his acknowledgement of Applicants' election without traverse of Group I, claims 1-4, 29 and 32, in Paper No. 13.

Priority

Applicants note that the Examiner has acknowledged Applicants' claim of priority to U.S.S.N. 60/166,336, filed November 19, 1999; U.S.S.N. 60/187,844, filed March 8, 2000; and U.S.S.N. 60/167,785, filed November 29, 1999. Applicants acknowledge that, for the above-referenced application, the priority claim to provisional application U.S.S.N. 60/187,844 is granted only for the specific polypeptide of SEQ ID NO:32 and its encoding nucleic acid.

Information Disclosure Statement

Applicants thank the Examiner for his acknowledgement of Applicants' information disclosures filed in Paper No. 7 on May 1, 2001; in Paper No. 8 on October 1, 2001; in Paper No. 10 on February 22, 2002; and in Paper No. 11 on April 22, 2002.

According to the Examiner, reference C14 of Paper No. 8, filed October 11, 2001, has not been considered "because this citation is not sufficient to indicate which application the search report is for and the referred search report could not be located in the file." Applicants have amended the citation for reference C14 on the enclosed Modified Form 1449/PTO. Applicants have also enclosed an additional copy of the C14 reference, the International Search Report for PCT/US00/31543, which was originally filed with the Patent and Trademark Office in Paper No.

8 on October 1, 2001. Although Applicants believe no additional fees are due with this resubmission, the Commissioner is hereby authorized to charge payment of any additional fees required in connection with the paper(s) transmitted herewith, or to credit any overpayment of same, to Deposit Account No. 50-0311, Reference No.15966-606 (CURA-106).

Specification Objections

The Examiner has objected to informalities in the specification, because the specification, at page 53, line 26, refers to "NOV14" under the heading and discussion regarding "NOV16." The specification has been amended herein to correct this discrepancy. Applicants, therefore, respectfully request that the Examiner withdraw this objection.

Claim Rejections

Rejection of Claims 1, 2, 29 and 32 Under 35 U.S.C. § 112, Second Paragraph

Claims 1, 2, 29 and 32 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1, 2, 4, 29 and 32 have been canceled. Accordingly, this rejection should be withdrawn.

Rejection of Claims 2, 4 and 45 Under 35 U.S.C. § 112, First Paragraph

Claims 2, 4 and 45 stand rejected under 35 U.S.C. §112, first paragraph for lack of written description.

Applicants traverse this rejection. First, claims 2 and 4 have been canceled. Second, claim 45 has been amended to recite a specifically limited group of polypeptide sequences, which are clearly described in the specification. Claim 45, as amended, has specific requirements for the polypeptide sequences that fall within it scope. The claimed sequences are limited to a polypeptide that is at least 95% identical to SEQ ID NO:32 and has an [ST]-x(2)-[DE] motif and kinase activity.

The present specification describes the claimed invention in "full, clear, concise and exact terms" that a skilled artisan would recognize that Applicants were in possession of the claimed

invention at the time the present application was filed. (*See e.g.*, page 50, lines 21-22; and page 53, line 24 through page 54, line 12). At pages 53-54, the specification discloses that polypeptides that include the amino acid sequence of SEQ ID NO:32 are members of a serine/threonine kinase family that can be defined by a stretch of highly conserved amino acid residues, [ST]-x(2)-[DE]. This motif is a requisite characteristic of polypeptides having kinase activity. Thus, the specification clearly describes the claimed invention, as claim 45 is directed to isolated polypeptides that contain the amino acid sequence of SEQ ID NO:32, including one or more kinase motifs, such that the claimed polypeptides exhibit kinase activity. These claims, therefore, are sufficiently described by the present specification, and Applicants respectfully request that the Examiner withdraw this rejection.

Claims 2, 4 and 45 also stand rejected under 35 U.S.C. §112, first paragraph for lack of enablement.

Applicants traverse this rejection. First, claims 2 and 4 have been canceled. Second, claim 45 has been amended to recite an isolated polypeptide that is at least 95% identical to the amino acid sequence of SEQ ID NO:32 and has an [ST]-x(2)-[DE] motif and kinase activity.

According to the Examiner, the specification is "enabling for a polypeptide comprising an amino acid sequence which is at least 95% identical to an amino acid sequence of SEQ ID: 32, wherein said polypeptide has kinase activity." (Office Action, page 7). Accordingly, claim 45 is enabled, and Applicants respectfully request that the Examiner withdraw this rejection.

CONCLUSION

On the basis of the foregoing amendments and arguments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

This application is now entitled to small entity status. The Commissioner is hereby authorized to charge payment of any additional fees required in connection with the paper(s) transmitted herewith, or to credit any overpayment of same, to Deposit Account No. 50-0311, Reference No.15966-606 (CURA-106).

Respectfully submitted,

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Dated: February 6, 2003

Version with Markings to Show Changes

In the specification:

On page 53, the paragraph beginning with line 24:

The encoded polypeptide has homology (approximately 43% identity) complement [receptpr] receptor 1 papio hamadryas (GenBank Accession. No Q29528). A search of the PROSITE database of protein families and domains revealed that a [NOV14] NOV16 polypeptide is a member of the serine/[theonine] threonine kinase family which can be defined by a polypeptide containing a stretch of highly conserved amino acid residues:

In the claims:

Claims 1, 2, 4, 29 and 32 have been canceled.

Claim 44 has been allowed.

Claims 46-49 have been added, and claim 45 has been amended as follows:

1. (Canceled)

2. (Canceled)

4. (Canceled)

29. (Canceled)

32. (Canceled)

44. (Allowed) An isolated polypeptide comprising an amino acid sequence of SEQ ID NO:32.

45. (Amended) An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to [an] the amino acid sequence of SEQ ID NO:32, wherein said polypeptide has the following characteristics:

(a) an [ST]-x(2)-[DE] motif; and;

(b) kinase activity.

-- 46. (New) A composition comprising the polypeptide of claim 44 and a carrier. --

-- 47. (New) A kit comprising, in one or more containers, the composition of claim 46. --

-- 48. (New) A composition comprising the polypeptide of claim 45 and a carrier. --

-- 49. (New) A kit comprising, in one or more containers, the composition of claim 48. --

TRA 1761501v1

Express Mail Label No. EV058119030US Date of Deposit: February 6, 2003

ATENT COOPERATION TREA

AJP C14

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

AUG 24 2001

To:
Mintz, Levin, Cohn, Ferris
Glovsky and Popeo, P.C.
Attn. ELRIFI, Ivor R
One Financial Center
Boston, MA 02111
UNITED STATES OF AMERICA

REGISTERED

Date of mailing (day/month/year) 20/08/2001	
Applicant's or agent's file reference 15966-606	PAYMENT DUE within 45 ~~months~~/days from the above date of mailing
International application No. PCT/US 00/ 31543	International filing date (day/month/year) 17/11/2000
Applicant CURAGEN CORPORATION et al.	

Done By
☐ Data Entry
☑ Docket Entry 16/11/01
☐ Docket Cross Off
☐ Previously Entered
☐ No Docketing Req
☐ ELITE
☐ Annuities

1. This International Searching Authority

(i) considers that there are 16 (number of) inventions claimed in the international application covered by the claims indicated ~~below~~/on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~/on the extra sheet:

(ii) [X] has carried out a partial international search (see Annex) [ ] will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

see Invention 1. on extra sheet

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby **invited,** within the time limit indicated above, to pay the amount indicated below:

EUR 945,00	x	15	=	EUR 14.175,00
Fee per additional invention		number of additional inventions		total amount of additional fees

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. [X] Claim(s) Nos. see remark have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mireille Claudepierre

Form PCT/ISA/206 (July 1992)

INVITATION TO PAY ADDITIONAL FEES

International application No.
PCT/US 00/31543

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-43, all partially

NOV1 polypeptide and variants thereof as illustrated by seq.ID.2, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

2. Claims: 1-43, all partially

NOV2 polypeptide and variants thereof as illustrated by seq.ID.4, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

3. Claims: 1-43, all partially

NOV3 polypeptide and variants thereof as illustrated by seq.ID.6, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

4. Claims: 1-43, all partially

NOV4 polypeptide and variants thereof as illustrated by seq.ID.8, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

5. Claims: 1-43, all partially

NOV5 polypeptide and variants thereof as illustrated by seq.ID.10, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

6. Claims: 1-43, all partially

NOV6 polypeptide and variants thereof as illustrated by seq.ID.12, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

7. Claims: 1-43, all partially

NOV7 polypeptide and variants thereof as illustrated by seq.ID.14, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

8. Claims: 1-43, all partially

NOV8 polypeptide and variants thereof as illustrated by seq.ID.16, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

9. Claims: 1-43, all partially

NOV9 polypeptide and variants thereof as illustrated by seq.ID.18, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

10. Claims: 1-43, all partially

NOV10 polypeptide and variants thereof as illustrated by seq.ID.20, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

11. Claims: 1-43, all partially

NOV11 polypeptide and variants thereof as illustrated by seq.ID.22, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

12. Claims: 1-43, all partially

NOV12 polypeptide and variants thereof as illustrated by seq.ID.24, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or

binding agent.

13. Claims: 1-43, all partially

NOV13 polypeptide and variants thereof as illustrated by seq.ID.26, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

14. Claims: 1-43, all partially

NOV14 polypeptide and variants thereof as illustrated by seq.ID.28, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

15. Claims: 1-43, all partially

NOV15 polypeptide and variants thereof as illustrated by seq.ID.30, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical compositions of said polypeptide, nucleic acid, antibody or binding agent.

16. Claims: 1-43, all partially

NOV16 polypeptide and variants thereof as illustrated by seq.ID.32, nucleic acids encoding them and fragments thereof, vector comprising said nucleic acid, cell comprising said vector, antibody against said polypeptide, use of the antibody or the nucleic acid in a detection assay for said protein resp. encoding nucleic acid, method for diagnosing a disorder associated with altered levels of said polypeptide resp. nucleic acid, method for identifying an agent wich binds to said polypeptide, and pharmaceutical

compositions of said polypeptide, nucleic acid, antibody or binding agent.

Human casein kinase II phosphorylation substrates are known from e.g. WO9518823. Human EGF-like proteins are known from e.g. WO9804688. Human fibrillin-like proteins are known from e.g. Ikegawa (1996) Genomics 35(3):590-92. The fact that some of the proteins of the application belong to one or more of the groups mentioned above can clearly not be considered as the special common technical feature.

In the light of this prior art, the problem underlying the present application has been defined as the provision of further human proteins and nucleic acids encoding them.
The solutions to this problem lie in the provision of NOV1-NOV16, as outlined above.

In view of the fact that casein kinase II phosphorylation substrates, EGF-like proteins, and fibrillin-like proteins are already known, due to the essential difference in primary structures and putative functions of the proteins of the solutions, and since no other special technical feature, common to these solutions could be distinguished, the ISA is of the opinion that there is no single inventive concept underlying the plurality of claimed inventions of the present application within the sense of Rule 13.1 PCT. Consequentely there is a lack of unity and the different inventions, not belonging to a common inventive concept, are formulated above as the different subjects on the communication pursuant to Art. 17(3)(a) PCT.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Although claims 23-28, 42-43, and claim 22 in as far as it partains to in vivo use, are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US 00/31543

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.
3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.
4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL [Online] Entry/Acc.no. AI613267, 26 April 1999 (1999-04-26) STRAUSBERG, R.: "ty35d07.x1 NCI_CGAP_Ut2 Homo sapiens cDNA clone IMAGE:2281069 3', mRNA sequence." XP002174078 the whole document ---	1-14,19
A	IKEGAWA SHIRO ET AL: "Structure and chromosomal assignment of the human S1-5 gene (FBNL) that is highly homologous to fibrillin" GENOMICS, ACADEMIC PRESS, SAN DIEGO, US, vol. 35, no. 3, 1996, pages 590-592, XP002155261 ISSN: 0888-7543 the whole document ---	
A	WO 98 04688 A (BECHTOLD ROLF ;BIOPHARM GMBH (DE); POHL JENS (DE); UNSICKER KLAUS) 5 February 1998 (1998-02-05) ---	
A	WO 95 18823 A (BETH ISRAEL HOSPITAL) 13 July 1995 (1995-07-13) ---	
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Form PCT/ISA/206 (Annex, first sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	NAGASE T ET AL: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES.17. THE COMPLETE SEQUENCES OF 100 NEW CDNA CLONES FROM BRAIN WHICH CODEFOR LARGE PROTEINS IN VITRO" DNA RESEARCH,UNIVERSAL ACADEMY PRESS,JP, vol. 7, 2000, pages 143-150, XP000943428 ISSN: 1340-2838 * see KIAA1482 * -----	5-7, 10-14, 19,30,33

1

Patent Family Annex

Information on patent family members

International Application No
PCT/US 00/31543

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9804688 A	05-02-1998	AU 4202897 A	20-02-1998
		EP 0922101 A	16-06-1999
		JP 2000516457 T	12-12-2000
WO 9518823 A	13-07-1995	US 5532167 A	02-07-1996
		US 6004757 A	21-12-1999